

Amendments to the Specification:

Please delete the paragraph beginning on page 8, line 13, which starts with "Brief description" and carries over to page 9.

Please replace the paragraph beginning on Page 9, line 6, with the following amended paragraph:

Total RNAs of rat tibialis anterior muscle and interscapular BAT were purified by the method described by Chomczynski et al. (*Anal. Biochem.* **162**, 156 (1987)). 1-2 µg of each RNA were reverse transcribed using oligo(dT)₁₅ primers and Moloney murine leukaemia virus (M-MLV) reverse transcriptase (Gibco BRL, New York, NY). Briefly, the RNA was mixed with 1.5 µl (150 ng) of oligo(dT)₁₅ in a total volume of 17.5 µl. The mixture was heated to 70°C for 10 min and cooled on ice. After a brief centrifugation, the RNA was reverse transcribed for one hour at 41°C (total volume 25 µl). The aliquots of first strand cDNA were stored at -20°C until use. The polymerase chain reaction was performed in a Perkin Elmer DNA Thermal Cycler 480 (Perkin Elmer, Lausanne, Switzerland). The first strand cDNA (2 µl) was amplified in a total volume of 50 µl in the presence of oligonucleotide primers corresponding, on rat UCP, to domains conserved between the species:

positions 279-298: CTGGACACCGCCAAAGTCCG (UCPRF) (SEQ ID NO:1)

positions 1021-1044: AGCACACAAACATGATGACGTTCC (UCPRR) (SEQ ID NO:2)

on GenBank Accession M11814. A unique fragment of similar size was obtained in the BAT and in the tibialis anterior muscle. The sequence of the BAT PCR product was identical to that of rat UCP, whereas the sequence of the tibialis anterior muscle PCR product was 60% identical to that of rat UCP. This fragment, called rat atypical UCP cDNA, was radioactively labelled with the nucleotide [α -³²P]dCTP and used as probe to screen a human skeletal muscle cDNA library (Stratagene, #936215, La Jolla, CA).

Please replace the first three full paragraphs on page 12, with the following three amended paragraphs:

~~As illustrated in Fig. 2A, a UCP2 signal 1.7 kb in size was detected in all the is~~
ubiquitously expressed in tissues studied. UCP2 is expressed at the highest level in BAT > white adipose tissue > skeletal muscle. In contrast, the expression of UCP3 (signal at 2.3 kb) is limited to the skeletal muscle and the heart. In the latter tissue, UCP3 is 10 times ~~less more~~ strongly expressed ~~than in~~ skeletal muscle (Fig. 2B). Direct comparison of the northern blots hybridized with the UCP2 and UCP3 probes showed that UCP3 is much more strongly expressed in skeletal muscle than UCP2. Probes specific for the long form or the short form of UCP3 showed that both forms give the same signal at 2.3 kb, and quantification of the intensity

of the signal showed that both forms are expressed at a similar level in human skeletal muscle (O. Boss et al., *FEBS Lett.* **408**, 39 (1997)).

The tissue distribution of UCP2 mRNA and UCP3 mRNA was also studied in rats using the rat atypical UCP cDNA probe, which hybridizes with the three species of rat UCP, UCP2 and UCP3 (O. Boss et al., *FEBS Lett.* **408**, 39 (1997)). ~~As illustrated in Fig. 2C, UCP2 is expressed in all the tissues studied: heart > BAT > white adipose tissue > skeletal muscle.~~ A major difference from human UCP2 is its high level of expression in heart. UCP3 is expressed at the highest level in BAT, at a high level in the tensor fascia latae (fast-twitch, glycolytic), tibialis anterior (fast-twitch, oxidative-glycolytic) and gastrocnemius (mixed) muscles and at a lower level in the soleus muscle (slow-twitch, oxidative). This suggests that UCP3 is more strongly expressed in the glycolytic than in the oxidative skeletal muscles. In rats, UCP3 was also detected, though at a much lower level, in the heart and kidney, and occasionally in the white adipose tissue.

~~It can be seen in Fig. 2C that t~~The UCP3 signal is a doublet whereas that of UCP2 is unique. The size of the messengers, compared with an RNA ladder, are 1.4 and 1.8 kb for UCP, 1.7 kb for UCP2 and 2.5 and 2.8 kb for UCP3.